Testimony of Gyula Acsadi, MD, PhD of Connecticut Children's Medical Center
to the Public Health Committee
Regarding HB 7282, An Act Concerning Newborn Screening for Spinal Muscular Atrophy
March 13, 2019

Senator Abrams, Representative Steinberg, members of the Public Health Committee, thank you for the opportunity to share my thoughts about HB 7282, An Act Concerning Newborn Screening for Spinal Muscular Atrophy.

My name is Dr. Gyula Acsadi, Division Head of Neurology at Connecticut Children's Medical Center. I am submitting this testimony in support of this proposed legislation because early (neonatal) diagnosis and treatment provides the best, most effective outcomes for children with spinal muscular atrophy.

Before commenting on the bill, I want to provide some background about Connecticut Children's. We are a nationally recognized, 187-bed not-for-profit children's hospital driving innovation in pediatrics. With over 2,600 employees and over 1,100 on our medical staff, we are the only hospital in the State dedicated exclusively to the care of children. Through our partnerships with adult hospitals and primary care providers across Connecticut, we are able to offer a continuum of care for children, from primary prevention to complex disease management, closer to their home. Last year alone, Connecticut Children's directly cared for more than 15% of all kids in Connecticut covered by Medicaid and spent over $90 million in free and uncompensated care. We are also the primary pediatric teaching hospital for the University of Connecticut School of Medicine and the Frank H. Netter MD School of Medicine at Quinnipiac University and the primary pediatric research partner of Jackson Laboratories.

Spinal Muscular Atrophy (SMA) is a genetic neuromuscular disease characterized by muscle atrophy and weakness. The most frequent form of disease (SMA Type 1) manifests early in life and is the leading genetic cause of death in infants and toddlers before two years of age unless invasive ventilator support is provided. SMA is caused by defects in the Survival Motor Neuron 1 (SMN1) gene that encodes the SMN protein. The SMN protein is critical to the health and survival of the large nerve cells (lower motor neurons) in the spinal cord responsible for muscle contraction leading to voluntary movements. Brain cells are not affected by this disease, and affected patients have normal intelligence.

SMA generally affects as many as 10,000 to 25,000 children and adults in the United States, and therefore it is one of the most common rare diseases. One in 6,500 children are born with this disease and one in 40 to one in 70 (approximately 6 million Americans) are carriers of the SMA gene. SMA is a recessive genetic disease, meaning that SMA carriers do not exhibit SMA

symptoms. If both parents are carriers of the SMA gene, then each of their children has a 1 in 4 chance of having the disease.

For decades there was no specific treatment of this disease. However, extensive research has led to several effective therapeutic options. The genetics of SMA provides a unique opportunity for therapeutic development. While SMA patients lack the functional SMN1 gene, they do have a "backup" gene, SMN2. SMN2 also makes the SMN protein, but at a greatly reduced efficiency, leading to lower than normal levels of the protein. SMN2 provides an attractive target for developing SMA therapeutics, and the majority of drug development efforts[1] in the field are focusing on increasing SMN protein production from this SMN2 gene. The other promising treatment is gene therapy, which is now under review by the FDA for treatment approval.

In December 2016, the FDA approved nusinersen (Spinraza), the first drug approved to treat children (including newborns) with adults with SMA. Nusinersen is an antisense oligonucleotide (ASO) designed to treat SMA. Several clinical trials and now at least two years of experience show that this treatment is effective by preventing decline, prolonging death and improving the functionality of patients. But this treatment is most effective if it is used very early or even before the first onset of symptoms.

Newborn screening is extremely effective in the early identification of SMA because 95% of SMA patients have the same genetic defect of deletion of a particular segment (exon 7-8) of the gene. Therefore, genetic testing and genetic based screening is easy to complete by means of a DNA-based assay.

In February 2018, the federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) recommended that newborn screening for SMA be implemented nationwide. This recommendation was subsequently approved by Health and Human Services Secretary Alex Azar in July 2018. There is universal agreement that early (neonatal) diagnosis and treatment provides the most effective, and sometimes normal functional outcomes for SMA patients. But in order to achieve this therapeutic result, Connecticut must implement a clinical strategy is to diagnose this progressive disease at birth by DNA-based neonatal screening.

Thank you for your consideration of our position. If you have any questions about this testimony, please contact Jane Baird, Connecticut Children's Senior Director of External Relations, at 860-837-5557.

[1] http://www.smafoundation.org/development/